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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/023,909	12/18/2001	Heather L. Davis	C1039/7058(HCL X04/19/02)	8458

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EXAMINER	
PARKIN, JEFFREY S	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 01/13/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/023,909	DAVIS ET AL.	
	Examiner	Art Unit	
	Jeffrey S. Parkin, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *03* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 October 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3 and 5-35* is/are pending in the application.

4a) Of the above claim(s) *2,3,5-7,15-19 and 34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5,8-14,20-33 and 35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/18/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Office Action

Status of the Claims

Acknowledgement is hereby made of receipt and entry of the communication filed 27 October, 2004, wherein claim 4 was canceled. This application contains claims 2, 3, 6, 7, 15-19, 34, and 36-98 drawn to an invention non-elected with traverse. A complete response to the final rejection must include cancellation of non-elected claims or other appropriate action (refer to 37 C.F.R. § 1.144 and M.P.E.P. § 821.01). Claims 1, 5, 8-14, 20-33, and 35 are currently under examination.

37 C.F.R. § 1.98

The information disclosure statement filed 18 November, 2004, has been placed in the application file and the information referred to therein has been considered.

35 U.S.C. § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

New Matter

Claims 1, 5, 8-14, 20-33, and 35 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed

invention. *In re Rasmussen*, 650 F.2d 1212, 211 U.S.P.Q. 323 (C.C.P.A. 1981). *In re Wertheim*, 541 F.2d 257, 191 U.S.P.Q. 90 (C.C.P.A. 1976). The claims have been amended to include the following limitation: "wherein the non-nucleic acid adjuvant is a **non-saponin** immune stimulating adjuvant". The crux of the statutory written description requirement is whether one skilled in the art, familiar with the practice of the art at the time of filing, would have found the later filed claimed limitations in the originally filed disclosure. *In re Wilder*, 736 F.2d 1516, 1520, 222 U.S.P.Q. 369, 372 (Fed. Cir. 1984). The specification clearly states (see p. 20) the following:

> "An immune stimulating adjuvant is an adjuvant that causes activation of a cell of the immune system. It may, for instance, cause an immune cell to produce and secrete cytokines. This class of adjuvants includes but is not limited to saponins purified from the bark of the Q. *saponaria* tree, such as QS21 (a glycolipid that elutes in the 21St peak with HPLC fractionation; Aquila Biophnrmaceuticals, Inc., Worcester, MA); poly[di(carboxylatophenoxy)phosphazene (PCPP polymer; Virus Research lnstitute, USA); derivatives of lipopolysaccharides such as monophosphoryl lipid A (MPL; Ribi Immunochem Research Inc., Hamilton, MT), muramyl dipeptide (MDP; Ribi) and threonyl-muramyl dipeptide (t-MDP,Ribi); 0M-174 (a glucosnmine disaccharide related to lipid A; OM Pharma SA, Meyrin, Switzerland); and *Leishmania* elongation factor (a purified *Leishmania* protein; Corixa Corporation, Seattle, WA)."

Thus, the skilled artisan would reasonably conclude that applicants contemplated using a large genus of non-nucleic acid adjuvants. However, the skilled artisan would not reasonably conclude from the teachings of the specification that applicants contemplated an immunization method that employed a "non-saponin immune stimulating adjvuant". The term is absent from the disclosure and nothing in the specification would lead the skilled artisan to this limitation. Accordingly, the skilled artisan would reasonably conclude that applicants were not in possession of the claimed

invention at the time of filing.

Enablement

Claims 1, 5, 8-14, 20-33, and 35 stand rejected under 35 U.S.C. § 112, first paragraph, because the specification does not reasonably enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. As previously set forth, the claims are broadly directed toward methods for the induction of antigen-specific immune responses in a subject through the administration of antigen and a combination of adjuvants comprising a CpG dinucleotide and a non-saponin immune stimulating adjuvant (e.g., MPL).

The legal considerations that govern enablement determinations pertaining to undue experimentation are disclosed in *In re Wands*, 8 U.S.P.Q.2d 1400 (C.A.F.C. 1988) and *Ex parte Forman* 230 U.S.P.Q. 546 (PTO Bd. Pat. App. Int., 1986). The courts concluded that several factual inquiries should be considered when making such assessments including the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims. *In re Rainer*, 52 C.C.P.A. 1593, 347 F.2d 574, 146 U.S.P.Q. 218 (1965). The disclosure fails to provide adequate guidance pertaining to a number of these considerations as follows: **1) The disclosure fails to provide adequate guidance pertaining to the structural requirements of any given ISS-ODN.** The skilled artisan would require a knowledge of those sequences that should be included in any given ISS prior to practicing the invention. However, the disclosure fails to provide sufficient guidance pertaining to the composition and length of those sequences that produce a synergistic immune response when combined with another adjuvant. Applicants' arguments and the declaration of Dr. Davis

failed to provide any objective evidence addressing this issue. While the declaration demonstrated that a combination of antigen (e.g., HBSag), CpG-1826, and art-recognized adjuvant provide a strong immune response, it failed to provide any detailed structural guidance pertaining to the structural requirements for any given ISS.

2) The disclosure fails to provide adequate guidance pertaining to those immune stimulating adjuvants (e.g., saponins, MPL, MDP, etc.) that can reasonably be expected to produce a synergistic immune response when combined with another adjuvant. Vaccine development is an empirical process that requires extensive experimentation to identify suitable combinations of immunogen and adjuvant(s), routes of inoculation, and immunization regimens. Moreover, the claims require a synergistic effect from combining the CpG-containing ISS and other non-nucleic acid adjuvant. While the declaration of Dr. Hunter provides some evidence for a synergistic immune response (e.g., CpG-1826, alum, and HBSag), it also demonstrates that many combinations of ISS, adjuvant, and immunogen were not synergistic. Thus, the skilled artisan would still needs to know which combination of CpG-ODN, non-nucleic acid adjuvant, and immunogen should be employed.

3) The prior art is unpredictable and teaches that many putative ISS elements do not function in the manner desired and often fail to facilitate immune responses to the immunogen of interest. Moreover, the skilled artisan cannot reasonably predict which combination of adjuvants will have a synergistic effect when employed concomitantly. The effectiveness of any given preparation will depend upon several factors including the antigen, adjuvants, dose, immunization regimen, and site of immunization. Because of the empirical nature of this process, the skilled artisan cannot reasonably predict which combinations of adjuvants will display synergistic effects when administered concomitantly with an

immunogen. This is not surprising considering the complexity of the immune system. As set forth *supra*, the declaration of Dr. Hunter delt primarily with a single ISS, CpG-1826. Thus, it failed to directly address this point.

4) The claims are of considerable breadth and are not fully supported by the disclosure. The broadest claims are not limited to any particular CpG-ODN or immune stimulating adjuvant or immunogen. Accordingly, the claims literally encompass tens-of-thousands of permutations. However, the disclosure, declaration, and applicants' arguments fail to teach which combination(s) of immunogen, CpG-ODN, and adjuvant will produce the desired response.

Accordingly, when all the aforementioned factors are considered *in toto*, it would clearly require undue experimentation from the skilled artisan to practice the claimed invention.

Finality of Office Action

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a). **A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.**

Correspondence

Any inquiry concerning this communication should be directed to Jeffrey S. Parkin, Ph.D., whose telephone number is (571) 272-0908. The examiner can normally be reached Monday through Thursday from 10:30 AM to 9:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner are unsuccessful, the examiner's supervisor, James C. Housel, can be reached at (571) 272-0902. Direct general status inquiries to the Technology Center 1600 receptionist at (571) 272-1600. Formal communications may be submitted through the official facsimile number which is (703) 872-9306. Hand-carried formal communications should be directed toward the customer window located in Crystal Plaza Two, 2011 South Clark Place, Arlington, VA. Applicants are directed toward the O.G. Notice for further guidance. 1280 O.G. 681. Informal communications may be submitted to the Examiner's RightFAX account at (571) 273-0908.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,

Jeffrey S. Parkin, Ph.D.
Primary Examiner
Art Unit 1648

07 January, 2005